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PAPILLO-CYSTOMA OF THE OVARY.

By T. S. Cullen, M. B., *Assistant in Gynecology.*

Although papilloma of the ovary is not particularly rare, this case is published on account of the involvement of both ovaries and because the places of origin are considered as being of interest. Moreover, as will be seen, the specimen was quite perfect.

Mrs. K., admitted to the service of Dr. Kelly, 2, 14, 1894. Æt. 41, married.

The patient complained of abdominal enlargement accompanied by loss of flesh and strength. She has been married 22 years and had one normal labor 20 years ago. Her only previous illness was typhoid fever, 10 years ago.

Present Illness.—In February, 1893, she began to feel languid, and was with difficulty able to continue her housework. In July she noticed a slight burning sensation in the right hypogastrium, not affected by exercise nor influenced by menstruation. Her body weight began to decrease. About September the abdomen commenced to enlarge and continued to increase in size. The weakness and emaciation also were progressive. In November she vomited a greenish fluid. Defecation was accompanied by some pain in the pelvis. Since that time there has been little change.

Menstruation commenced in her eleventh year, was regular, moderate in amount and somewhat painful. In November, *the menses suddenly ceased* and have not recurred.

Physical Examination.—The patient is fairly well nourished. Her mucous membranes are somewhat anæmic. Heart and lungs apparently normal. Liver dulness not increased. The abdomen is enormously and symmetrically distended. The greatest prominence is below the umbilicus. The lineæ albicantes in the lower abdominal zone are very prominent. The superficial veins are distended.

Palpation.—Some superficial œdema above the symphysis pubis. No masses to be felt.

Percussion.—No tympanitic note can be elicited below the umbilicus. A distinct wave of fluctuation is felt. Above the umbilicus the tympany extends 16 cm. to the right and 12 cm. to the left of the median line.

Abdominal Measurements.—

Umbilicus to ensiform cartilage	21 cm.
" " pubes	27 "
" " right anterior superior spine	27 "
" " left anterior superior spine	27 "

Greatest circumference 145 cm., at the umbilicus.

Vaginal Examination.—The outlet is greatly relaxed. The cervix is in the axis of the vagina; uterus retroflexed, apparently fixed in the pelvis. No tumor felt.

Per rectum.—In Douglas's pouch a mass of indefinite size can be detected, conveying the impression of small papillomatous masses.

2, 17, 1894. Operation by Dr. Kelly, double cystectomy. On opening the abdomen 17 litres of fluid were found free in

the cavity. On both sides large cysts were seen, occupying Douglas's cul-de-sac; by these the uterus was pushed forward. The left side was elevated, tied off and removed without difficulty. The right side was enucleated after being liberated from dense adhesions to the broad ligament and to the posterior surface of the uterus. Adhesions between the bladder and broad ligament were cut, and about eight small papillary nodules were excised from the pelvic floor. It was impossible, however, to remove all of them on account of their intimate relation to the bowel. The peritoneum was thoroughly sponged out and the wound closed. Silk sutures were used throughout. During the third week the temperature rose to 101.8° and fluctuated between that and 99.5° for three days, otherwise the patient had an uninterrupted recovery, and was discharged on March 20, feeling well.

Pathological Report.—Right side, the ovary is replaced by a tumor 8.5x8x7 cm. This is irregular in contour, being made up of several cysts, varying in size. These cysts are bluish-white and translucent. The most dependent part of the tumor is yellowish in color. Springing from the uterine side of the tumor is a pinkish cauliflower-like mass which has a somewhat narrowed base. The interior of the tumor is occupied by five cysts; these are smooth-walled, but have, developed upon their inner surfaces, small papillary-like masses. The fluid in the large cyst is somewhat tenacious, in the smaller ones limpid. The tube is 4 cm. long, 5 mm. in diameter. Its fimbriated end is free. Parovarium is normal.

Microscopically.—The cyst walls are composed of connective tissue moderately rich in cells. Several corpora fibrosa are scattered throughout the wall. The outer surface is lined by flat epithelium. The papillary masses springing from the outer surface are composed of finger-like projections of connective tissue which become branched toward their termination. The connective tissue near its attachment to the cyst wall is moderately rich in cells, but as it passes outward the cells diminish in number and the stroma presents a hyaline appearance. The surface epithelium as it approaches the papillary masses becomes cuboidal, and where covering the masses is cylindrical. The inner surface of the cyst wall is lined by cylindrical epithelium. The papillary masses springing from the interior, Fig. 3, present the same appearance as those on the outer surface, but appear to have no connection with them.

Left Side.—The ovary is converted into a similar tumor of the same size; here, however, the papillary masses tended to spring from the depressions between the cysts. Both tubes normal.

Source of Origin.—The outer ones undoubtedly spring from the germinal epithelium. It is the opinion of Professor Welch that those on the inner surface of the cysts originated in the cells of the Graafian follicles; the cysts forming first, and the papillary masses developing secondarily. This mode of origin is, we consider, indicated by the small number of cysts present. The small masses from the tissue surrounding the rectum presented a typical papillary appearance.

Professor Abel made a chemical examination of the fluid from the abdominal cavity. The fluid was yellowish in color and presented a greenish tinge, was alkaline in reaction and had a specific gravity of 1020. It contained serum albumen, serum globulin, a trace of sugar and fibrin.

Although the prognosis in this case was considered unfavorable owing to the incomplete operation, the patient has, during the six months following the operation, gained 49 pounds.

The sudden cessation of menstruation is of especial interest as associated with the diseased condition of the ovaries.

Description of Plate.

Fig. 1.—Natural size of tumor from right side, hardened in Müller's fluid and then cut open. Springing from its outer surface are papillary masses. Internally it is composed of one large and several smaller cysts. Projecting from the inner surface of these are papillary masses. The large cyst, *c*, contains a tenacious fluid which was coagulated by the Müller's fluid. *a* is a cross section of the normal Fallopian tube.

Fig. 2 is the other half of Fig. 1. The coagulated fluid has been washed out of the large cyst cavity, enabling one to see the papillary masses more distinctly.

Fig. 3 is a section of a small nodule taken from the inner surface of the cyst in Fig. 1 at the point represented by *b*. (Winckel Ocul. I, Obj. 3.) *d* is the cyst wall, which is composed of wavy fibrous tissue poor in blood supply. The inner surface of the cyst is covered by one layer of cylindrical epithelium. The papillary mass presents a tree-like appearance. It also is composed of connective tissue, which becomes less dense the farther it is away from the cyst wall. All the folds and convolutions of this papillary mass are covered by one layer of cylindrical epithelium. In some places the cells have been cut slantingly and then look somewhat like squamous epithelium. The orange-colored areas are blood-vessels.

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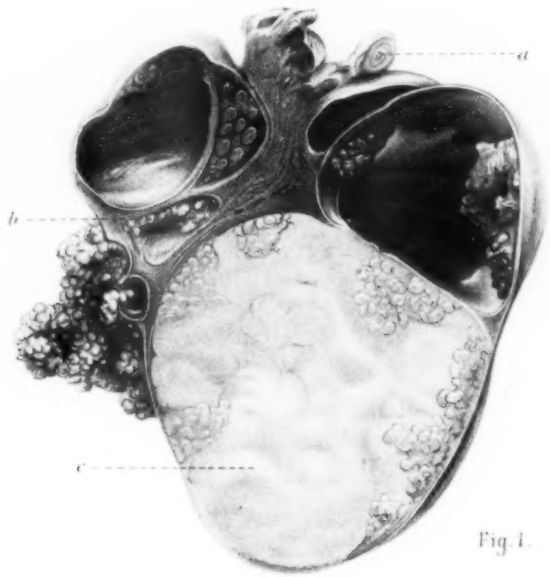
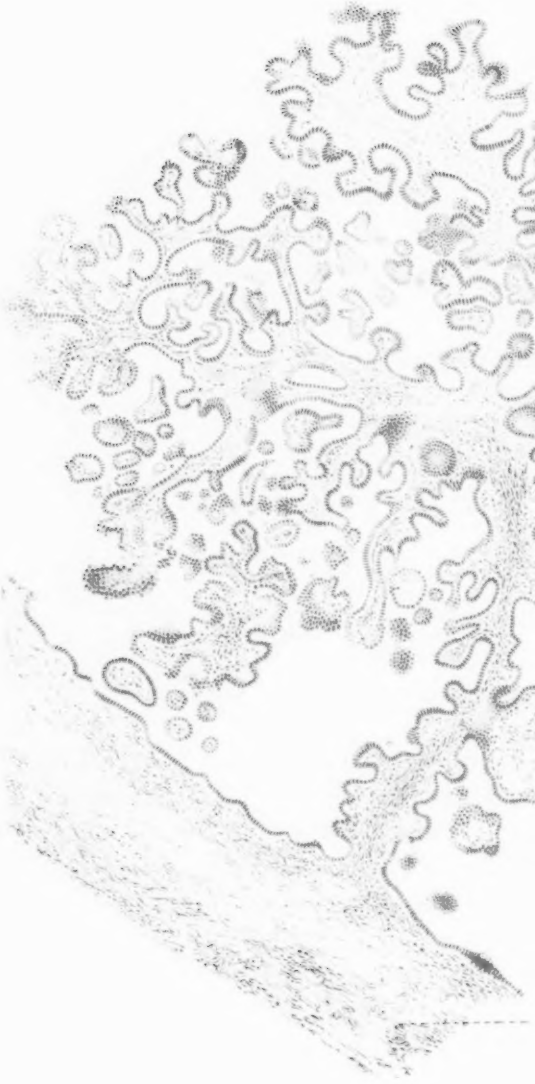


Fig. 1.

Fig. 2.

M.Broödel del.



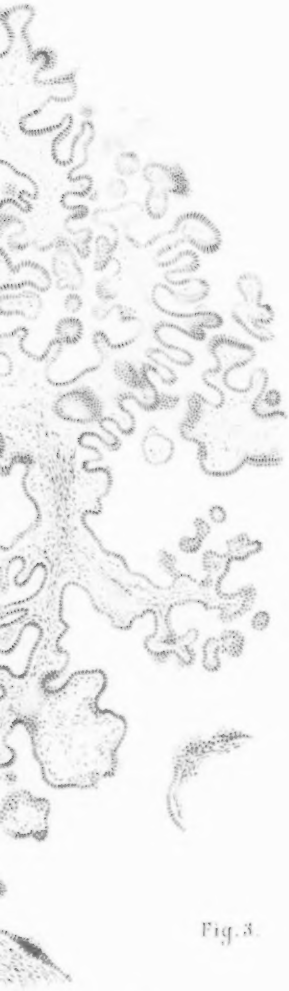


Fig. 3.

d

THE LEUCOCYTES IN CROUPOUS PNEUMONIA.

BY JOHN S. BILLINGS, JR., *Assistant Resident Physician, Johns Hopkins Hospital.*

The increase in the number of leucocytes in the blood in croupous pneumonia may be said to have been first noticed by Piorry[1] in 1839. He remarked that the so-called "crusta phlogistica," seen above the clotted blood withdrawn by venesection from patients suffering from any of the acute inflammatory diseases, was most marked in pneumonia. It was thickest at about the seventh or eighth day, just before the crisis, and he thought it to be due to an hæmitis or an actual inflammation of the blood itself.

Virchow[2] in 1871 spoke of a leucocytosis in pneumonia and held that there was an actual new formation of leucocytes, *i. e.* an absolute increase in the total number present in the circulation, but only in those cases in which there was swelling of the bronchial glands.

Since then there have been many investigations on the subject, especially in the last four years. Nasse,[3] Koblanck, Sörensen and Pée all noted the presence of a leucocytosis during the course of croupous pneumonia, but they did not speak of its relation to the temperature, nor to prognosis.

Halla[4] in 1883 was the first to report a series of cases, fourteen in number. In twelve of these there was a leucocytosis, while in the remaining two the leucocytes were not increased. Both the latter cases ended fatally. He was the first to call attention to the fact that the absence of leucocytosis is of bad omen. He found no correspondence between the temperature and leucocyte curves in those cases ending in recovery.

Hayem and Gilbert[5] in 1884 remarked upon the typhoid character of those cases of pneumonia in which there is no leucocytosis.

Tumas[6] in 1887 stated that there was a rough daily correspondence between the temperature and the leucocytes, and that the number of the latter was greatest at the severest stages of the disease. He also noted that the leucocytes did not reach normal at the same time as the temperature, but remained elevated for three or four days after the crisis.

Boekmann[7] and Von Jaksch[8] claim that there is a constant relation between the number of leucocytes and the temperature in various acute infectious diseases, and particularly in pneumonia.

Kikodse[9] states that leucocytosis is absent only in fatal cases. He believes that the leucocytosis begins before the involvement of the lung takes place, that it runs parallel with the temperature, and falls to a point below normal with the crisis in temperature.

Roemer[10] believes the leucocytosis in pneumonia to be caused by the products of destruction (bacteria, cells, etc.) brought about by the alkali-proteins, and not directly by the alkali-proteins themselves.

Von Jaksch,[11] recognizing the bad prognosis in cases which showed no leucocytosis, and believing that the fatal termination was due directly to its absence, recommended the use of drugs which would produce an increase in the number of leucocytes in the blood. (Antipyrin, pilocarpin, etc.) Such treatment was ineffectual, as will be demonstrated later.

Maragliano[12] does not think that the number of leucocytes is of any prognostic value.

Rieder[13] reports his observations in twenty-six cases. He finds that the fall of the leucocytes generally precedes the fall of temperature, but that the number of the leucocytes, while beginning to fall first, may often remain elevated for several days after the temperature has touched normal. This is particularly marked in cases of delayed resolution. In cases ending by lysis the leucocytes fall correspondingly slowly. A pseudo-crisis may be recognized by the fact that while the temperature may fall to normal, the leucocytes remain steadily elevated. He finds no correspondence of the leucocyte and temperature curves. The leucocytosis was present in one case six hours after the chill. In fatal cases there was no leucocytosis, but the blood showed the characteristic change noted in so-called pure leucocytoses, *i. e.*, a marked relative increase in the number of so-called polynuclear elements. He does not think there is any relation between the amount of leucocytosis and extent of lung involved.

V. Limbeck[14] holds that only those infectious diseases with exudation into the tissues show an increase in number of the leucocytes. The amount of leucocytosis depends upon the quality and quantity of the exudate, *i. e.*, the more cells and the larger the exudate, the greater the leucocytosis. He states that in pneumonia the leucocytosis disappears with the fever. Should there be a new extension of the disease and a rise of fever, the leucocytosis reappears a few hours before the rise in temperature takes place. A pseudo-crisis may be recognized by a steady leucocytosis. A fatal ending is foreshadowed by a steady rise in the number of the leucocytes.

Tchistovitch[15] inoculated rabbits with cultures of pneumococcus and found a leucocytosis only in those cases ending in recovery. The use of stronger cultures which killed the animal did not cause any leucocytosis, but brought about an actual reduction in the number of the leucocytes, *i. e.*, a so-called leukolysis. This was confirmed by Rieder (l. c.).

Laehr[16] reports observations of the leucocytes in sixteen cases of pneumonia. He found the leucocytosis in one case to be present eight hours after the chill. The leucocytes rise one to two days before the crisis, to sink again before the crisis takes place. The temperature reaches normal before the leucocytes. He finds no exact correspondence between the number of leucocytes, the fever and the amount of lung involved, but thinks they do correspond roughly. He believes the leucocytosis to be due to chemotaxis, the attracting substances being the alkali-proteins, etc., produced by the pneumococcus. Persistence of the leucocytosis signifies delayed resolution of the pneumonic consolidation, and its reappearance indicates a recurrence of the disease.

Schulz[17] states that the leucocytosis observed in pneumonia, as well as all other inflammatory leucocytoses, is not due to any absolute increase in the number of leucocytes in the circulation, but only an altered division. He believes that in health the large abdominal vessels contain many more leuco-

cytes ("Wandständig") than the peripheral vessels. In disease the presence of abnormal chemotactic substances in the blood, and the increased rapidity and force of the respiration and circulation, are enough to drive these extra leucocytes out into the circulation and to those points where they may be needed.

Rovighi[18] states that in pneumonia the leucocytes reach their highest point during the period of fall of temperature. He bases this statement on the results of experiments going to show that when the body is heated the number of leucocytes in the peripheral circulation diminishes, while cooling the body increases their number. These are purely local phenomena, not due in any way to changes on the part of the blood-making organs.

Cabot[19] reports observations in seventy-two cases of pneumonia. Seven of these ended fatally, and six out of the seven showed no leucocytosis. In one case ending in recovery, which showed no leucocytosis at first, there was a steady rise in the number of the leucocytes towards the end of the disease. He does not think that there is any relation between the amount of leucocytosis, the degree of severity of the case, and amount of lung involved.

Ewing[20] reports a number of cases, and draws the following conclusions. 1. The greater the amount of lung involved, the greater the leucocytosis. 2. The amount of leucocytosis corresponds to the "systemic reaction," the latter being judged by the temperature, pulse and general condition of the patient: *i. e.*, in fatal cases there is no leucocytosis, and *vice versa*. 3. A well marked leucocytosis indicates a severe infection, a low leucocytosis is unfavorable, and the absence of any leucocytosis makes the prognosis very grave.

Tchistovitch[21] reports the results of some further inoculation experiments upon animals. As is well known, the inoculation of animals with certain substances (tuberculin, sterile culture of staph. py. aur., and pilocarpin) produces first a temporary leukolysis (so-called), which is followed by a marked leucocytosis. He found that those substances which produce a leucocytosis in healthy rabbits do not do so when injected into rabbits previously inoculated with virulent cultures of pneumococcus. The progressive diminution of the leucocytes caused by the latter substance steadily continues, or at most there is only a slight transient leucocytosis, which is followed by a fresh fall. He holds this to show that those cases of pneumonia which succumb to the great virulence of the specific pneumococcus, should show no leucocytosis, and that no stimulant of leucocytosis should be able to produce any leucocytosis in such cases. So that the presence of a leucocytosis in fatal cases of pneumonia should make us doubt that the virulence of the specific pneumococcus was the cause of death, and we should seek some other cause of death in such cases, such as extensive involvement of the lungs or localization of the disease in the heart or in the brain.

When he injected the pneumococcus culture into the brain of the animal there was produced a meningo-encephalitis with a marked rise in the number of leucocytes in the blood. The amount of culture used was just so much as, injected elsewhere in the body, would bring about a severe infection with leukolysis, but without fatal termination. In conclusion, he holds that the presence or absence of leucocytosis only shows the virulence of the poison and is not a criterion of absolute prognosis.

He saw four fatal cases of pneumonia. In one there was no leucocytosis. Of the other three, all of which showed a leucocytosis, one had endocarditis and meningitis, another meningitis, while the third case showed extensive consolidation of both lungs.

Bieganski[22] reports a series of cases, paying especial attention to the relative numerical proportions of the various forms of leucocytes. In cases showing a marked leucocytosis, 80 to 90 per cent. of the leucocytes are polynuclears, while the eosinophiles and blood-plates are practically absent. Just after the crisis in temperature the polynuclears sink to below 60 per cent., while the eosinophiles and blood-plates reappear in increased numbers, about three days being taken for the blood to return to its normal condition. In fatal cases the polynuclears are reduced to 50 per cent. or below. Such a condition of the blood together with an absence of leucocytosis makes the prognosis unfavorable.

He holds that the leucocytosis in pneumonia is due to a lessened destruction of the polynuclear forms. This is brought about by the toxines of bacterial origin which are circulating in the blood. The mononuclear elements are unaffected and continue to enter the circulation and to develop there into polynuclears. Here all progress ceases and there is neither any destruction of the polynuclears with formation of blood plates, nor further development of the polynuclears into eosinophiles. In the fatal cases the toxines are supposed to have a paralyzing effect upon the development of all the forms of leucocytes, and also to prevent the entrance of young forms into the circulation.

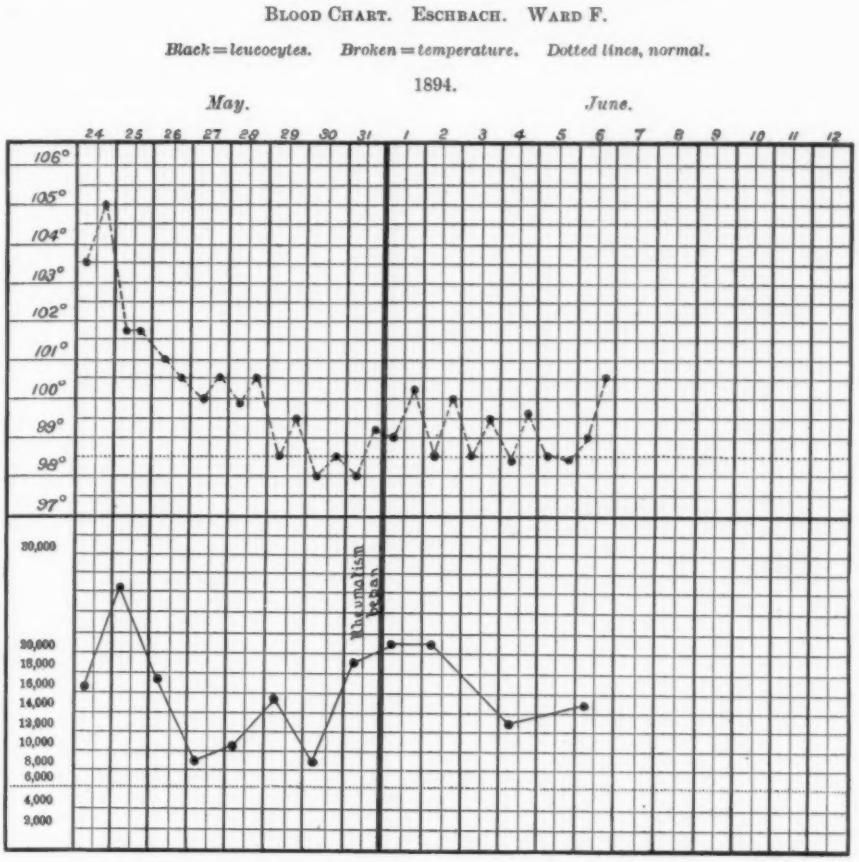
The twenty-two cases here reported were not picked ones, excepting that eight or ten were thrown out, either because too few counts were made or because the crisis in temperature occurred within twenty-four hours after entry into hospital. The methods and precautions used in counting the blood, and in examining and preparing dried and stained specimens, were exactly the same as those employed in the investigations of the leucocytes in malarial fever reported by the writer in the October number of this journal for 1894.

In each case charts were made of the leucocyte and temperature curves, so that comparison of the two could readily be made. Three of these charts are reproduced in this article. The leucocytes were counted on an average of twice a day during the febrile period.

Cases.

1. W. R., æt. 26. Illness lasted 12 days. Right middle, right lower and left lower lobes involved. Temperature ranged high until sixth day, when it fell by lysis, taking 6 days to reach normal. Leucocytes 39,500 six hours after chill. No daily correspondence with temperature curve; they reached their highest point (50,000) two hours after temperature began to fall. Thenceforth they fell steadily, reaching normal one day after temperature.

2. S. F., æt. 51. Illness lasted 8 days. Right middle and lower lobes involved. Temperature ranged at 102° for 6 days; fell by lysis, reaching normal in 50 hours. Leucocytes 42,000



CASE 4. PNEUMONIA AND RHEUMATIC FEVER. SHOWING FALL BY LYSIS.

8 hours after chill. They fell steadily until temperature began to fall, when they rose sharply to 38,000, reaching normal 2 days after temperature.

3. H. H., æt. 22. Illness lasted 17 days. Right middle and lower lobes involved, with delayed resolution. Temperature fell on seventh day of disease, to rise again sharply to 102°. Fell again by lysis, reaching normal in 5 days. Leucocytes ranged between 20,000 and 28,000 until the day the temperature touched normal, when they began to fall, reaching normal eleven days after temperature.

4. R. E., æt. 42. Illness lasted 9 days. Right middle and lower lobes involved. For temperature and leucocytes see chart. Leucocytes reached highest point (27,000) during period of fall of temperature. They reached normal at the same time as the temperature. Two days afterwards P. was taken with acute rheumatic fever, with a simultaneous rise of temperature and leucocytes. P. still had rheumatism when discharged at his own request.

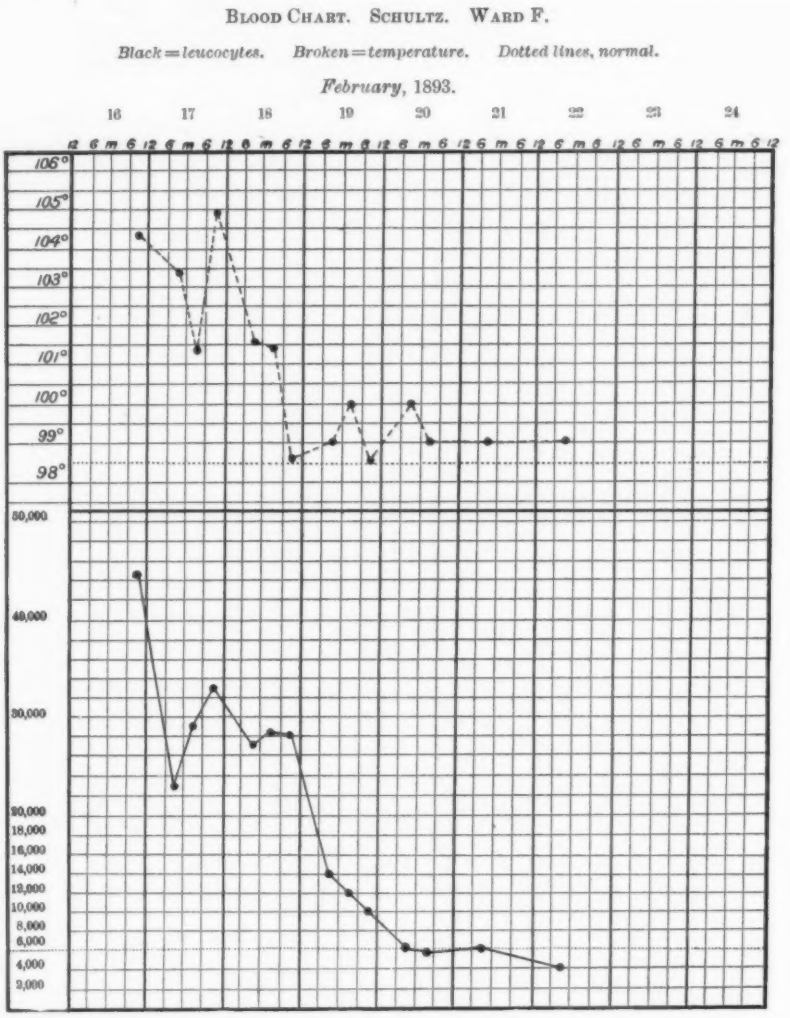
5. J. S., æt. 13. Illness lasted 6 days. Right middle and lower lobes involved. For temperature and leucocytes see chart. Leucocytes rose during fall of temperature, but had reached their maximum before that time. They reached normal 36 hours after temperature, the crisis in which took 24 hours.

6. E. W., æt. 7. Illness lasted 9 days. Left lower lobe involved. Temperature ranged high until 8th day, when there was a pseudo-crisis, the temperature rising sharply afterwards. Crisis took place the following morning, lasting 2 hours. Leucocytes ranged at 24,000 until the true crisis took place, when they began to fall, but did not reach normal until two days after temperature.

7. G. S., æt. 40. Alcoholic history. Illness lasted 7 days. Left upper lobe. Temperature ranged at 105 until 5th day, when it began to fall, reaching normal in 36 hours. Leucocytes ranged very low during whole course of disease, reaching their maximum (13,000) during the period of fall of temperature. This, together with the history and situation of disease, made the prognosis a grave one, but patient made an uninterrupted recovery.

8. E. F., æt. 20. Illness lasted 8 days. Right middle and lower lobes were involved, with delayed resolution. Temperature ranged high until the 7th day, when it fell by crisis, reaching normal in 10 hours. Leucocytes ranged at about 25,000 until crisis in temperature, when there was a slight fall to 16,000, followed by a gradual rise to 27,000, the leucocytes not reaching normal until 7 days after temperature.

9. C. J., æt. 30. Patient was admitted for tertian malarial fever. Lungs were clear on admission, and the pneumonia



Case 5. Pneumonia. Showing fall by Crisis.

began 36 hours later. For temperature and leucocytes see chart. Quinine was given on the evening of the chill, and the malarial organisms rapidly disappeared, and with their disappearance the number of leucocytes rapidly increased. There was successive involvement of the right lower, right middle and left lower lobes, each fresh extension of the disease being followed by a sharp rise in the number of the leucocytes. Leucocytes reached highest point (68,000) just before the fall in temperature began, and thenceforth decreased in number, reaching normal 6 days after temperature.

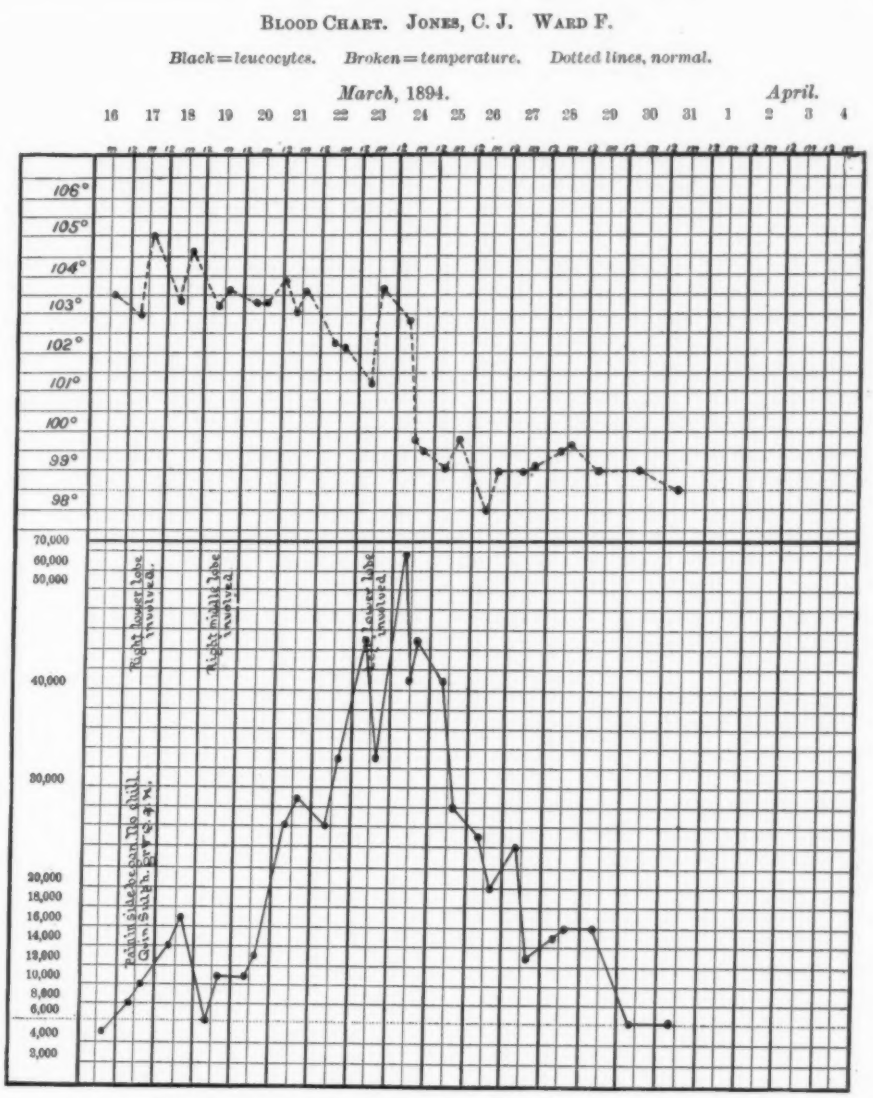
10. E. M., æt. 45. Illness lasted 10 days. Left upper lobe involved. Temperature ranged at 103° until 9th day, when it fell by crisis, reaching normal in 16 hours. Leucocytes reached maximum (36,000) two days before crisis. They fell with temperature, but did not reach normal until two days after crisis.

11. C., æt. 26. Illness lasted 13 days. Right upper, middle and lower lobes involved. Temperature ranged at 104° until 11th day, when it fell by crisis, reaching normal in 48 hours. Leucocytes low on admission; reached maximum (29,000) during period of fall of temperature. Did not reach normal until 7 days after temperature.

12. L. K., æt. 24. Illness lasted 8 days. Right lower lobe involved. Temperature ranged high until 8th day, when it fell to normal in 24 hours. Leucocytes ranged at 25,000 until crisis in temperature occurred, when they fell to 16,000, but rose again to 29,000 (maximum). They did not reach normal until 8 days after temperature. Delayed resolution.

13. J. H., æt. 41. Illness lasted 10 days. Right upper lobe involved. Temperature ranged between 102° and 104° until day of death, when it fell, being 100° 2 hours before death. Leucocytes 22,000 on admission, rose to 38,000 that p. m., falling steadily afterwards. 10,000 just before death. No autopsy.

14. J. W., æt. 73. Illness lasted 8 days. Right upper, middle and lower lobes involved. Temperature ranged at



CASE 9. PNEUMONIA AND MALARIA. SHOWING FALL BY CRISIS.

101° until 30 hours before death, when it rose to 104°. Leucocytes ranged at 25,000 from admission until death. Autopsy. In addition to pneumonic consolidation above noted, P. had an acute fibrino-purulent meningitis due to the dip. pneumoniæ.

15. G. W., æt. 25. Illness lasted 10 days. Right upper, middle and lower and left lower lobes involved. Temperature ranged from 101.5° to 104°, being 104.2° at death. Leucocytes 8,000 on admission, rose steadily until time of death 8 days later, when they were 30,000. Autopsy showed the pneumonic consolidation above noted. No meningitis nor endocarditis.

16. K. D., æt. 47. Illness lasted 4 days. Right upper and middle lobes involved. Temperature ranged at 102.5° until death, with a pseudo-crisis to 99° 12 hours before death. Leucocytes 18,000 on admission, where they ranged until death. 15,000 just before death. No autopsy.

17. C. L., æt. 36. Illness lasted 21 days (?). Lower lobes of both lungs involved. Temperature ranged steadily at 102° until 12 hours before death, when there was a pseudo-crisis to 99°, with a sharp rise to 103° just before death. Leucocytes 13,000 on admission, fell gradually to normal in two days. They began to rise 36 hours before death, reaching 32,000 just before the end. No autopsy.

18. J. C., æt. 63. Illness lasted 11 days. Right middle and lower lobes involved. Temperature ranged at 103.5° until 2 days before death, when it rose to 106.2°, falling to 104° just before death. Leucocytes 8,000 on admission. Remained normal until day before death, when they rose to 20,000, falling to 14,000 before death. No autopsy.

19. F. S., æt. 50. History of alcoholism. Illness lasted 24 days (?). Right upper and middle lobes involved. Temperature ranged at 104° during the four days preceding death.

The afternoon of the fourth day the P., being left alone for a moment, climbed through the top of a window and fell to the ground outside, breaking vertebral column and both bones of right leg. Unsatisfactory coroner's inquest showed nothing beyond the fractures and the pneumonic consolidation above noted. Leucocytes 15,000 on admission; for the first 3 days fell gradually to 11,000, but after the accident above referred to, rose to 18,000. P. lived 4 hours after the accident occurred.

20. H. L., æt. 41. Illness lasted 5 days. Right lower base involved. Temperature on admission 102.5°. For next three days it ranged at 104°, being 103.8° just before death. Leucocytes 10,000 on admission, after which time they ranged steadily below normal; from 6,000 to 1,500. They were 4,000 just before death. No autopsy.

21. A. N., æt. 47. Illness lasted 12 days. Lower lobes of both lungs involved. Temperature ranged from 103.5°–105°, until shortly before death, when it rose to 107°. Leucocytes 15,000 on admission; 2 days later they rose to 28,000. Ranged at 22,000 until just before death, when they touched 30,000. No autopsy.

22. A. P., æt. 22. Illness lasted 3 days. Left lower lobe involved. Temperature ranged steadily at 103° until death. Leucocytes 50,000 on admission; fell steadily, being 20,000 when death occurred. Autopsy showed beside a double lobar pneumonia, an acute nephritis and fatty degeneration of heart muscle, together with hemorrhage into pericardial sac, with the presence of dip. pneumoniæ.

Of these twenty-two cases, twelve recovered and ten died. Of the twelve favorable cases, four ended by lysis and eight by crisis.

Taking up first the four cases ending by lysis, we see that in all there was a marked leucocytosis at some period of the disease. Examination of the combined leucocyte and temperature charts showed that before the temperature began to fall there was no daily correspondence between the two curves. In all four cases the two curves began to fall together, the leucocytes not reaching normal until one, four and fourteen days after the temperature in cases 1, 2 and 3 respectively. In case 3 there was delayed resolution of the consolidation, it not having entirely cleared up on discharge.

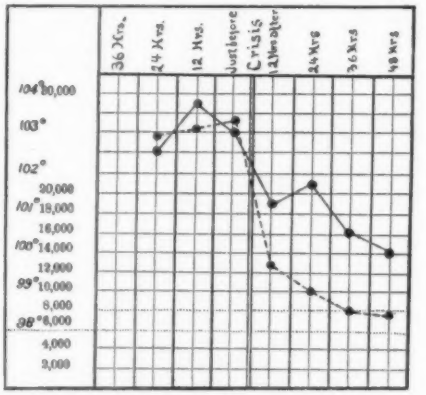
In cases 1 and 3 the leucocytes reached their maximum during the period of fall of temperature. There was a sharp rise during that period in case 3, but the maximum had been reached before the temperature began to fall.

In case 1, where there was involvement of both lungs, the leucocytes reached 50,000. In the other three cases the lower portion of the right lung was involved and the range of the leucocyte curves was moderate, being above 30,000 in only one instance.

In cases 1, 2 and 4 the fall in temperature preceded the fall of leucocytes.

Case 4 is interesting on account of its complication with rheumatism. The combined chart is given and it shows well the correspondence of the two curves. The occurrence of a moderate leucocytosis during the course of rheumatic fever has been mentioned by several observers. In cases 1 and 2 the leucocytes were 39,500 and 42,000 6 and 8 hours after the chill, respectively.

Of the eight cases ending by crisis, in all but one there was a marked leucocytosis during the febrile period of the disease. In the remaining case the leucocytes, while ranging at normal during the greater period of the disease, touched 13,000 on one occasion. [Case 7.] Examination of the combined charts showed no daily correspondence of the two curves before crisis occurred. The leucocytes began to fall before the temperature in three cases, with it in two, and after it in three. The fall of leucocytes was only partial in six cases, however, and they did not reach normal until from two to eight days after the temperature. In cases 6 and 7 the leucocytes and temperature reached normal at the same time. In cases 7, 9, 11 and 12 the leucocytes reached their maximum during the period of fall of temperature. In cases 5 and 8 there was a rise of leucocytes during that period, but the maximum had been previously attained. Most of these points are well shown in a combined chart of the eight cases, showing the average temperature and number of leucocytes, twelve, twenty-four and thirty-six hours before and after the crisis in temperature.



Black = leucocytes. Broken = temperature.

CHART SHOWING TEMPERATURE AND LEUCOCYTE CURVES OF PNEUMONIA. CRISIS.

In case 9 the lower portions of both lobes were involved and the leucocytes touched the highest point reached in any of the cases, viz., 68,000. In case 11 however, where there was the same extent of involvement, the leucocytes only reached 29,000. In case 7 only the left upper lobe was involved and the leucocyte range was practically normal, only once being above 10,000. The prognosis in this case was thought to be grave at first on account of the absence of leucocytosis, the position of the consolidation, the alcoholic history and patient's age. The patient made an uninterrupted recovery however, and the infection was evidently a very mild one. In the other five cases only a portion of one lung was involved and the leucocyte curve ranged moderately high.

In only one of the eight cases was it possible to count the blood before and after the chill. This was case 9, in which the pneumonia came on while patient was being treated for malarial fever of the double tertian type. In the article on the leucocytes in malarial fever, previously referred to, the

fact is brought out that in malarial fever the leucocytes range constantly below normal during the course of the disease. This is due in some way to the presence of the malarial organism in the blood. It is not settled as to whether it is a leukocytolysis (an actual destruction of leucocytes) or a leukopenia (a diminished production). Now in case 9 there was no leucocytosis either before or after the chill, until the exhibition of quinine caused the disappearance of the malarial organisms from the blood, when the leucocytes promptly rose. It is interesting to note how, as each new portion of the lung was involved, there was a corresponding rise in the number of the leucocytes. [See chart.]

Of the ten fatal cases only one (No. 20) showed a complete absence of leucocytosis during the entire course of the disease. In cases 16 and 19 the leucocytes, while being always above normal, ranged relatively low, never being above 19,000. In case 14 the leucocytes behaved as one would expect them to in an uncomplicated case ending in recovery. In cases 15, 17 and 21 the leucocytes were practically normal on admission, but gradually rose during the ensuing three or four days, touching just before death 30,000, 32,000 and 30,000 respectively. In cases 13 and 22 the leucocytes were high on admission, but fell steadily from that time on until death. In case 18 they were normal for the first two days, but rose sharply to 20,000 24 hours before death, falling slightly just before the end.

Thus we see that in fatal cases the behavior of the leucocytes varies widely. In six cases there was absence of leucocytosis at some period of the disease, but the continuous absence is the exception, not the rule. In none of the cases was there any daily correspondence between the temperature and leucocyte curves. In the four cases in which the leucocytes rose at the end however, there was a corresponding rise in temperature. As regards the relation of the amount of leucocytosis to the extent of lung involvement, no definite conclusions can be drawn. In case 15, where the entire right lung and a portion of the left were involved, the maximum leucocytosis was only 30,000 just before death. None of the cases were seen until at least twenty-four hours after the chill, so that no data are furnished as to how early the leucocytosis appears.

Autopsies were obtainable in only three out of the ten cases. This does not include the coroner's inquest on case 19. The results of these autopsies bear out Tchistovitch's statements however. In case 14, where the leucocytes ranged above 20,000, an acute fibrino-purulent meningitis was found to be present. In case 15, where the leucocytes ranged from 17,000 to 30,000 for 5 days, extensive involvement of both lungs was found. In case 22, where the leucocytes ranged from 50,000 to 20,000, there was found at autopsy double lobar pneumonia, acute nephritis, fatty degeneration of the heart muscle, and hæmorrhage into the pericardial sac, with the presence of the diplococcus pneumoniæ in the latter situation. In case 19, where the leucocytes ranged at 18,000, the fracture of the spine was probably the immediate cause of death. In case 21 there was involvement of both lungs, with a leucocyte range above 20,000. All the remaining cases, with the exception of No. 13, showed a low range of leucocytes, and it is only fair to consider it possible that in case 13 also, an autopsy might have revealed some complication or condition accounting for the relatively high leucocytosis.

There are a number of theories as to the cause of leucocytosis. Virchow held that it was due to proliferation within the lymph glands, that it only occurred in those cases of disease associated with glandular enlargement; also that acute glandular enlargement was followed by leucocytosis. This is negatived by the absence of leucocytosis in many diseases accompanied by glandular enlargement (tuberculosis, acute Hodgkin's disease, etc.), and by the presence of marked leucocytosis in diseases associated with very slight glandular enlargement. [Pneumonia.] Every leucocytosis is probably associated with some glandular enlargement however. Such a leucocytosis as Virchow supposes would be a lymphocytosis, which is not the case.

Schulz's theory has been already mentioned. Its falsity would seem to be proved by the work of Goldscheider and Jacob (to be referred to later), who found that in cases showing a leucocytosis in the peripheral circulation, there was no corresponding diminution in the leucocytes in the central blood-vessels.

Römer (l. c.) thinks the increase due to direct multiplication (by amitosis) of the leucocytes, the exciting cause of such multiplication being the destruction-products of the alkali-proteins, as has been mentioned. He thinks chemotaxis to play a large part. No such changes as he infers are to be made out in the blood.

Von Limbeck (l. c.) holds leucocytosis to be due to the action ("Fernwirkung") of the bacterial products themselves upon the leucocytes. He does not speculate as to the source from which the increase is drawn.

Bieganski's theory has been mentioned. Too little is known about the so-called blood-plates and eosinophiles to justify us in drawing conclusions from any variations in their number. Most authorities deny that the blood-plates are end-products of the polynuclear leucocytes.

Löwit[23] holds that every leucocytosis is preceded by a diminution in the number of leucocytes. This is due, he thinks, to an actual destruction of the leucocytes, and he calls it leukolysis. This leukolysis is in turn followed by a pouring forth of young elements from the hæmatopoietic organs. This reparation far exceeds the destruction, in this way bringing about a leucocytosis. He demonstrates by injection experiments that the artificially-produced leucocytosis is preceded by a leukolysis. His ideas as to the source from which the increase is drawn would seem to be negatived by the absence of evidence of new formation. Were new formation to occur, the blood would show a large number of young elements. This it does not do.

The latest work on the subject is that of Goldscheider and Jacob[24]. They make use of the terms hypo- and hyperleucocytosis for leukolysis and leucocytosis respectively. Their conclusions are as follows: Hypoleucocytosis is due to the leucocytes being driven into and detained within the capillaries of certain organs of the body. Actual destruction plays a minor rôle. Hyperleucocytosis is due to an increased quantity of leucocytes being carried to the blood by the lymph stream.

There is no new formation of leucocytes, its absence being offset by the supposition that in the bone-marrow and spleen there are a large number of adult leucocytes held in reserve, as it were, which are carried off by the lymph stream into the general circulation when occasion arises. The occurrence of new formation is negatived by the absence of young forms in dried specimens.

All these phenomena are primarily due to the bacterial products or chemical substances in the blood. In most acute infectious diseases these substances are introduced into the circulation slowly and cause no diminution in number of the leucocytes, the latter rising immediately. This statement is borne out by experiment. This would mean that in pneumonia the leucocytosis would be found to be present at the time of the chill.

The authors are led to believe that the sources of the leucocytosis are the blood-making organs. But there is no evidence of new formation; hence their theory of a reserve force of adult leucocytes within those organs. This theory seems rather to be constructed to meet the necessity of the case than to be founded on sufficient evidence.

Sherrington[35] in a recent article reports observations of his own on inflammatory leucocytosis. He discusses most of the prevailing ideas, but formulates no new theory.

It is beyond the province of this article to enter into any further discussion of these theories. All we can say is that the leucocytosis in pneumonia is probably due in some way to the products of the diplococcus pneumoniæ. While the bacteria do not enter the blood as a rule, their products do, and in this way can influence the various organs of the body. There is probably no new formation of leucocytes, or at any rate it plays a minor rôle in the process, and some other source for the increase in number of the leucocytes must be sought for.

The behavior of the leucocytes depends upon the virulence of the bacterial products. In fatal cases where the virulence is great, a rise in the number of leucocytes is rendered impossible. It is doubtful whether there is any actual diminution of their number, there being no evidence that actual destruction of leucocytes takes place. The virulence may be so modified as to permit of a gradual increase in number of the leucocytes, yet still be potent to cause death. Cases may begin favorably and the leucocytes may range high at first; the virulence of the bacterial products may then increase, causing a gradual reduction of the leucocytes, and death. The sharp rises sometimes observed just before death may be associated in some way with the pre-agonal leucocytoses. We must not forget that the disease may be present in so mild a form that the leucocytes are unaffected and remain normal throughout. This is shown in case 7 of our series. Most of the above points are shown in the following table:

1. Very mild infection: No effect on leucocytes. Normal range.

2. Moderate infection: Moderate leucocytosis.

3. Severe infection (as to extent of lung involvement): Marked leucocytosis.

4. Severe infection (as to virulence of bacterial product): Moderate leucocytosis.

5. Very severe infection: No leucocytosis.

It has not been proved, as will be shown later, that the blood condition in the fatal cases differs in any way from the normal as regards the relative numerical proportions of the various forms of leucocytes.

If this be true, it is easy to see that the examination of the blood in pneumonia is not of absolute prognostic value. The blood only furnishes an indication of the virulence of the bacterial products; the extent of lung involvement, the general condition of the patient, and the temperature must also be taken into account in every case. For instance, should we be guided by the blood condition alone, our prognosis in cases coming under the heads of 1 and 5 in the above table would be either favorable or unfavorable according to the view we took. The error would of course be fatal.

The absence of leucocytosis in the fatal cases is evidently not the cause of death. Hence the failure of Von Jaksch's treatment by injecting such substances as would produce a leucocytosis in the healthy individual.

Regarding the question of the variations of the various forms of leucocytes, too much time was taken up by the actual counting to allow of much work in this direction. Twenty counts were made in the various cases showing a marked leucocytosis, with the following average result: Polynuclears, 91.2 per cent.; mononuclears, 9.6 per cent.; eosinophiles, 0.2 per cent. Three counts were made in cases showing no leucocytosis, and the results were practically those which would have been obtained in counting the leucocytes in normal blood, thus agreeing with neither Rieder nor Bieganski.

	Polynuclears.	Mononuclears.	Eosinophiles.
(*a*)	71.8 per cent.	28.2 per cent.	0
(*b*)	73.5	26.1	0.4 per cent.
(*c*)	76.1	23.4	0.5

Count (*c*) was in case 18. As has been mentioned, the leucocytes rose sharply just before death. A count was made two hours before death and the increase was found to be in the polynuclears solely. Polynuclears, 95.4 per cent.; mononuclears, 4.3 per cent.; eosinophiles, 0.3 per cent.

These counts would seem to make it doubtful that Bieganski's conclusions hold. The number of counts however, is too small to have any weight.

Conclusions.

1. In cases of pneumonia pursuing a favorable course there is, as a rule, a marked increase in the number of the leucocytes during the febrile period of the disease. This leucocytosis is probably present at the time of the chill, and may be very marked within a few hours. There is no correspondence between the daily temperature and leucocyte curves during the febrile period.

2. In those cases in which the temperature curve falls by crisis, the leucocyte curve begins to fall within a few hours of the same time. The fall of the latter is only partial however, and rarely reaches normal as soon as the temperature curve, generally taking about 48 hours longer. In cases ending by lysis the two curves fall together, the temperature always reaching normal first. In cases of delayed resolution the leucocytes may remain elevated for days.

3. In a majority of the cases the leucocyte curve rises during the period of fall of temperature, and may reach its maximum at that time. Such a rise is only transient, however, and is soon followed by a fresh fall.

4. In cases showing extensive involvement of both lungs, the leucocytes are apt to reach a higher point than in those cases where the involvement is only moderate. The correspondence of lung involvement and amount of leucocytosis is a very rough one however.

5. The fatal cases may show either the presence or absence of leucocytosis. In those cases showing a leucocytosis, some other cause of death than the virulence of the bacterial poison must be sought for.

6. The prognosis in cases showing a complete and continuous absence of leucocytosis is unfavorable as a rule. A continuous absence of leucocytosis is the exception, most cases showing a leucocytosis at some period of the disease. The possibility of the absence of leucocytosis being due to extreme mildness of the disease must not be overlooked.

7. The leucocytosis in pneumonia is a so-called pure leucocytosis, *i. e.* an increase in the polynuclear elements solely. In cases showing no leucocytosis, the blood condition according to the observations here reported, is normal. Further investigations are necessary before the work of previous observers can be positively contradicted.

8. The presence or absence of leucocytosis only shows the virulence of the bacterial poison. It is not a criterion of absolute prognosis.

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A POSTSCRIPT TO THE REPORT ON APPENDICITIS.*

BY W. S. HALSTED, M. D., *Surgeon-in-Chief, etc.*

Dr. Finney's remarks on the treatment of the wound in cases of appendicitis have been abbreviated so much as possibly to mislead those who are not familiar with our methods. When he speaks of "leaving the abdominal wound open" he means that the wound is drained with gauze, and not that no attempt is made to close it. The fact is that the wound is sewed up tight about the gauze, so tight that it is sometimes necessary to cut one stitch in order to remove the packing. Whenever pus is encountered either within the appendix or outside of it the wound is drained. Sometimes one or two narrow strips of gauze are sufficient, sometimes very many broad strips are required. Ordinarily all of the gauze is brought out at one point and between stitches which, as I have said, embrace it snugly. The gauze is used not only for drainage, but quite as much to stimulate adhesions between the coils of intestine which surround it and thus effectually shut off the general peritoneal cavity from its infected portion. The gauze is gently packed about the stump of the appendix, and should reach into every recess of the pus cavity. When the abscess is a large and ramifying one, or when there are several abscesses, we may bring the gauze packing out of the abdomen at more than one point in the wound.

These wounds are closed with mattress sutures; but the sutures are not always buried as they are in all uninfected abdominal wounds which are completely closed and in which the danger of stitch infection is not so great. The stitches, where they are not buried, are prevented from cutting into the skin by pieces of rubber tubing or of gauze. These wounds should be stitched with great care. All of the divided tissues (the peritoneum excepted) should be included in each stitch unless the stitches are buried. Inasmuch as the muscles retract unevenly the sewing is sometimes a difficult task. If the wound is sewed in this way, and if sufficient care is exercised to avoid the infection of the stitches as they are being introduced and tied, there is little if any danger that a hernia will ensue.*

Even the point at which the gauze traverses the abdominal wall is not a weak one. A connective tissue membrane, the wall of the obliterated sinus, extends from the stump of the appendix to this point in the wound and binds the intestines to

*See Johns Hopkins Hospital Bulletin, June-July, 1894.

*At the meeting of the Johns Hopkins Medical Society, November 5, 1894, I presented a case of appendicitis to illustrate our treatment of the incision. Buried sutures of silver wire had been used to bring together the cut edges of the abdominal muscles, and an uninterrupted buried suture of silver wire closed the wound in the skin. The latter suture had already been withdrawn and a fine pink line indicated where the skin incision had been made. A little below the centre of the wound was the orifice of a sinus from which a narrow strip of gauze had just been removed. The cicatrix was three weeks old.

each other, and to the underside of the lips of the open part of the wound. The thickness of this membrane depends principally upon the length of time that the gauze is allowed to remain undisturbed. I have found it so strong after ten days that I could with difficulty thrust my finger through it. This membrane atrophies in time. After two years I have found the walls of a sinus to the gall bladder attenuated to little more than a trace.

With our present resources it is not justifiable to attempt to disinfect an abscess cavity of the peritoneum, no matter how infinitesimally small this abscess may be. Bull and two others, whose names I am not at liberty to mention, are probably not the only ones who have furnished disastrous instances of such attempts.

In operations for appendicitis we have always the strangulated stump of the appendix and usually tissues more or less necrotic in its immediate vicinity as a complication. My experiments* demonstrated conclusively the result of inoculation of strangulated tissues in the peritoneal cavity.

The problem is a very different one when we have an abscess in the cancellous tissue of bone or in highly vascular soft parts to deal with. We may safely close such abscess cavities. If, for example, the so-called pyogenic wall of an abscess in muscle is excised and the parts are then thoroughly washed with an antiseptic solution, we may so far inhibit the pyogenic organisms that the tissues or, if there is a dead space, the prolific granulations, assisted possibly by the blood, may altogether destroy them. In the cancellous tissue of bone a cavity large enough to hold a hickory nut becomes completely filled with granulations in about three days. Blood clots occupying such cavities, if inoculated with virulent cultures of staphylococcus aureus, rarely break down. As a rule, the so-called organization of the clot takes place in from two to four days without suppuration. But an abscess in the peritoneal cavity is a very different affair because (1) the wall of the abscess consists in part of strangulated or more or less necrotic tissue which we cannot excise; (2) attempts to disinfect such an abscess would probably be futile and might be worse than futile; (3) failure to disinfect might mean general peritonitis and the death of the patient, and not merely the retardation of healing.

There cannot be a definite incision for appendicitis. In general, if there is a large abscess, the incision should be made as near as possible to the crest of the ileum, so as to diminish the chances of entering the clean peritoneal cavity and to lessen the possibility of a hernia. The muscles are thick in this region, and when divided offer broad surfaces for coaptation by suture; and if the incision is too close to the ileum to admit of suture there is little danger of hernia resulting, as we know from a long experience with psoas abscesses, which we open by preference in this region. But the position of the abscess or, if there is no pus or too little pus to be detected, the position of the appendix in the given case should determine the site of the incision. If there is an abscess the tissues over it should be most carefully studied as they are being incised for signs of infiltration with inflammatory products. A little œdema of the deeper muscles (transversalis or internal oblique) may guide us to a circumscribed spot of adhesion of cæcum or omentum to parietal peritoneum and enable us to empty a large abscess without entering the uninfected part of the peritoneal cavity, or to thoroughly protect the intestines about the encapsulated pus cavity from the danger of infection before the pus is liberated. We place several yards of gauze between the healthy intestines and the abscess before opening the latter.

From a bacteriological point of view, we must often, if not always, inoculate the healthy peritoneum, but thus far we have not in a single instance had peritonitis supervene upon an operation for appendicitis, nor have we a single death to attribute to the operation. In the case of a large abscess, which we have evacuated without entering the uninfected peritoneal cavity, we still hesitate to search for and remove the appendix if its removal would necessitate our entering the clean peritoneal cavity.

When there is little or no pus to be discovered we make our incision directly over the appendix, which can usually be palpated. Here, too, we try to cut through thick muscles if possible. The instant that the peritoneum is opened, and before it is widely incised, we introduce large towels of gauze, and with these press the intestines over the appendix out of the way and towards the left. When the appendix is nicely exposed and a clear field for operation obtained, we introduce more gauze to serve as an inner lining to the outer ring of gauze. The adhesions which bind down the appendix are then slowly broken up by gentle finger pressure, and if pus is present it is caught as it leaks out by additional gauze sponges. If the inner layer of gauze packing should by accident become soiled it is immediately replaced by fresh packing, the opening into the abscess being meanwhile stopped with a gauze sponge. And so, little by little, the abscess is emptied, and finally the appendix removed. After ligating the appendix and its mesentery we may excise the mucosa which is cut off by the ligature. We never sew up the end of the stump in the infected cases, as some surgeons have advised. This would be a foolish waste of time; for the circulation of the part stitched has been cut off by the ligature applied to the appendix. The gauze for packing is rubbed full of a mixture of iodoform and bismuth and then sterilized.

*The Johns Hopkins Hospital Reports. Report in Surgery, I.

THE JOHNS HOPKINS HOSPITAL REPORTS.

Volume IV, No. 6 (Report in Surgery II), Now Ready.

CONTENTS: THE RESULTS OF OPERATIONS FOR THE CURE OF CANCER OF THE BREAST, PERFORMED AT THE JOHNS HOPKINS HOSPITAL FROM JUNE, 1889, TO JANUARY, 1894.

By WM. S. HALSTED, M. D., *Professor of Surgery, Johns Hopkins University, and Surgeon-in-Chief to the Johns Hopkins Hospital.*

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THERAPEUTIC USE OF EXTRACT OF BONE MARROW.

BY JOHN S. BILLINGS, JR., *Assistant Resident Physician.*

(*Read before the Johns Hopkins Hospital Medical Society, November* 5, 1894.)

The use of bone marrow in cases of anæmia and in certain diseases of the blood-making organs was probably suggested by the success of the treatment of myxœdema with thyroid extract. The marrow is thought by most authorities to be the principal seat of formation of the red blood corpuscles. A diminution in number of the red corpuscles may be due to increased destruction or to diminished formation, and it was hoped that in either case the administration of the marrow as a medicine would stimulate the blood-making organs to increased activity, and thus make up the loss in red corpuscles.

The first case of anæmia treated in this manner was reported by Fraser.[1] A diagnosis of pernicious anæmia was made, based upon the history of the case, the number of red corpuscles and per cent. of hæmoglobin, and the poikilocytosis of the red corpuscles. No mention was made as to the occurrence of nucleated red corpuscles, the presence of which in the blood in pernicious anæmia being a point upon which Ehrlich lays considerable stress. The case was given bone marrow with arsenic for the first two months, then bone marrow alone for a month, and finally bone marrow and iron for three months. In the first two months the corpuscles rose from 1,000,000 per cmm. to 4,000,000, ranging at the latter point until discharge, four months later.

Bigger[2] reports a case of leucocythæmia in a boy, which was treated with the bone marrow. There was rapid diminution in the size of the spleen and marked improvement within a week. No mention is made of any examination of the blood, and it is possible that the case may have been one of splenic anæmia or of the pseudoleukæmic infantile anæmia of Von Jaksch.

Danforth[3] reports a case of pernicious anæmia apparently cured by the use of bone marrow. Here also the report of the blood condition is incomplete, as only the number of red corpuscles and per cent. of hæmoglobin are stated. The latter rose from 35 per cent. to 80 per cent. The bone marrow in this case, as in that of Fraser, was given in combination with arsenic.

In our own cases the marrow was given in the form of a glycerin extract which was prepared in the following manner. Twelve sheep's ribs, carefully scraped, were chopped into small fragments and rubbed up in a mortar with one pound of glycerin. This was allowed to macerate for three or four days, being kept in a refrigerator during that time. It was then strained through gauze, and the resultant liquid administered in teaspoonful doses three times a day. No complaint was made by the patients with regard to its taste.

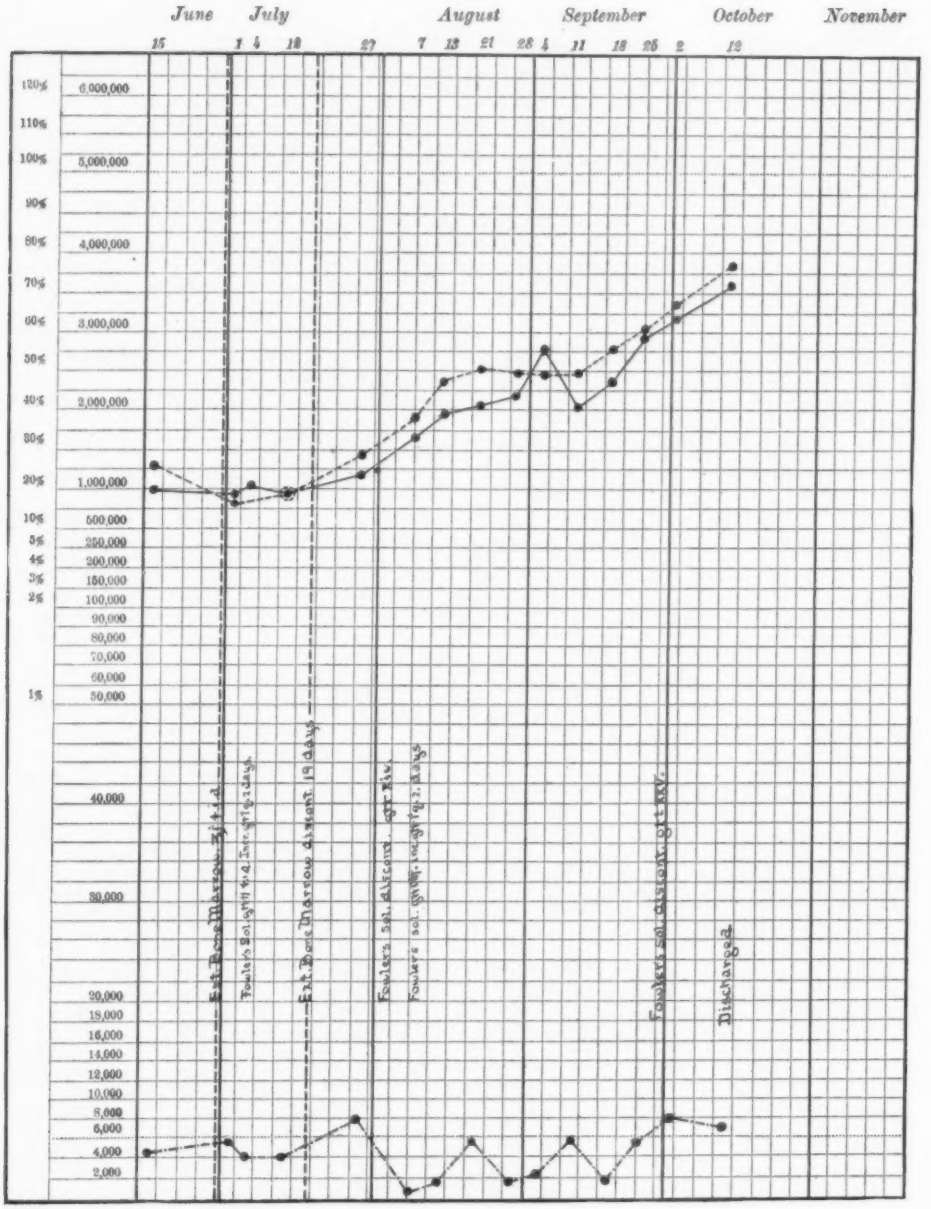
Case 1.—Chlorosis. Girl, aged 20; admitted June 21, 1894, complaining of dyspnœa and weakness. Past history was negative. Present illness of four months' duration. Physical examination showed nothing beyond marked anæmia, and a loud functional murmur along the left sternal margin.

Blood count on admission, reds 2,898,000, whites 5000; hæmoglobin 32 per cent. Stained specimens of the blood showed nothing beyond the pallor of the centre of the red corpuscles, so characteristic of chlorosis. No treatment was instituted for the first ten days, *i. e.* until July 1st, when the extract of bone marrow was begun. The blood count at that time was, reds 3,198,000, whites 5500; hæmoglobin 38 per cent. The extract was discontinued July 16, as patient insisted on leaving the hospital. The blood count on the morning of discharge was, reds 4,192,000, white 7000; hæmoglobin 40 per cent. She was given Blaud's pills, and subsequently did well.

Case 2.—Chloro-anæmia in a boy. Past history was negative. For a month had complained of headache and gradually increasing weakness. Inspection showed a moderate grade of anæmia, physical examination being otherwise negative. On admission the blood count was, reds 3,290,000 per cmm.; hæmoglobin 35 per cent. Stained specimens of the blood showed nothing beyond the pallor of the centre of the red corpuscles. Such a blood condition in a young female would certainly lead to a diagnosis of chlorosis, but the diagnosis of chlorosis in the male is always hazardous. The extract of marrow was ordered, and the condition of the blood gradually improved, the red corpuscles reaching a normal point (5,000,000 per cmm.) in about a month. The hæmoglobin rose more slowly, and on discharge (see chart 3) was only 68 per cent. As a rule, in chlorosis we must be satisfied if we can get the hæmoglobin as high as 75 to 80 per cent.

Case 3.—Pernicious anæmia. Man, aged 51, admitted June 15, 1894, complaining of vomiting and progressive weakness. He was very pale, and had first noticed the pallor ten weeks before. Had not lost very much in weight. Inspection showed a marked grade of anæmia, with the lemon-yellow discolorization of the skin so frequently seen in pernicious anæmia. Physical examination and examination of the stomach contents were negative. The case was at first suspected to be one of cancer of the stomach, but the absence of tumor, the readiness with which the gastric symptoms yielded to treatment, and finally the condition of the blood, all pointed to its being a case of the idiopathic anæmia of Addison, the so-called primary pernicious anæmia. Blood count on admission, reds 1,148,000, whites 4430; hæmoglobin 27 per cent. By July 1st the red corpuscles had sunk to 918,000, and the hæmoglobin to 17 per cent. Stained specimens showed marked poikilocytosis and polychromatophilic staining of the red corpuscles. Several nucleated red corpuscles seen, the greater number being normoblasts. The remainder were typical megaloblasts, with large pale nuclei and polychromatophilic protoplasm. Many micro- and megalocytes. A differential count of the leucocytes showed the per cent. of the small mononuclear forms or lymphocytes to be increased to 34 per cent., almost twice the normal. This technical description of the blood condition is given to show the grounds on which the diagnosis was based. The absence of any apparent causative factor, and the fact that the per cent. of hæmoglobin was relatively higher than that of the red corpuscles, confirmed the diagnosis. The use of the extract of bone marrow was begun June 30th. At first the blood condition improved, the red corpuscles rising to 1,400,000. They fell again to 970,000, however, and the extract was discontinued July 18th, it having been given 19 days without causing improvement. Fowler's solution was ordered in increasing doses, and the patient gradually improved, being discharged October 12th in fairly good condition. Blood count on discharge, reds 3,600,000, whites 7000;

[1] Brit. Med. Jour., June 2, 1894.
[2] Lancet, September 22, 1894.
[3] Chicago Clin. Review, IV, 1894.



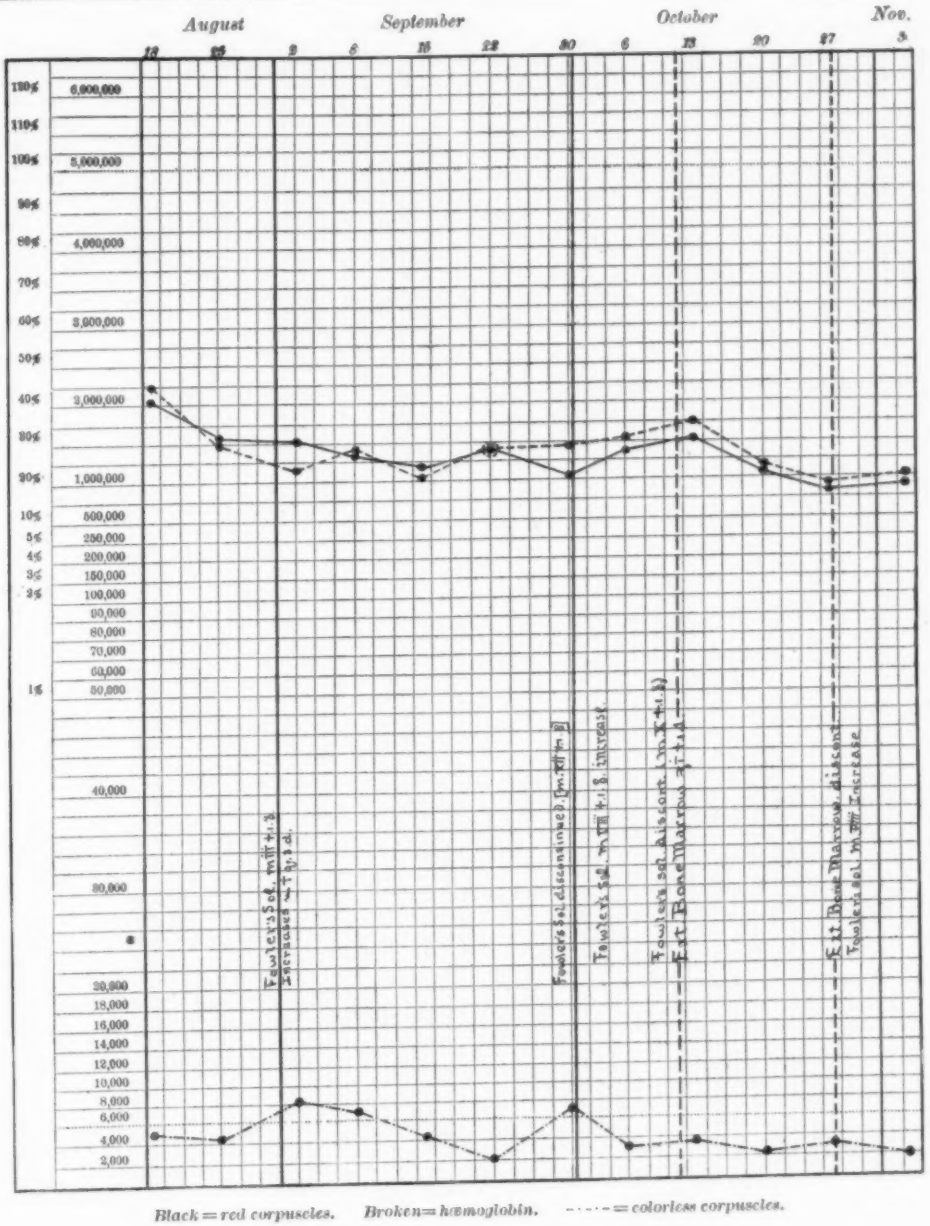
Black = red corpuscles. Broken = hæmoglobin. ·-·-·-= colorless corpuscles.

No. 1. J. K. Pernicious Anæmia. Case 3.

hæmoglobin 69 per cent. Stained specimens showed no poikilocytosis, no nucleated red corpuscles, and the per cent. of the various forms of leucocytes was normal. (See chart 1.)

Case 4.—Pernicious anæmia. Man, aged 65, admitted August 15, 1894, complaining of weakness and shortness of breath. Illness began about one year before admission, and has been gradually progressive ever since. Has lost very little weight. Physical examination negative beyond a marked grade of anæmia. Skin distinctly lemon-tinged. The urine was high-colored, but of low specific gravity, a condition which has been frequently observed in pernicious anæmia, and which is supposed by Hunter to be due to the presence of pathological urobilin in the urine. The recent investigations of Hopkins (Guy's Hosp. Rep., 1893) would seem to make the existence of this substance improbable. He found only normal urobilin and hæmatoporphyrin in the urine in pernicious anæmia. Blood count August 18, reds 2,048,000, whites 5000; hæmoglobin 45 per cent. Stained specimens showed a moderate grade of poikilocytosis, such as is seen in severe secondary anæmia. No nucleated red corpuscles. Percentages of leucocytes normal. The number of red corpuscles gradually sank, and between September 8th and October 6th ranged between 1,120,000 and 1,392,000; during this time patient was taking Fowler's solution.

Stained specimens of the blood taken September 2d showed marked poikilocytosis, many micro- and megalocytes and many polychro-

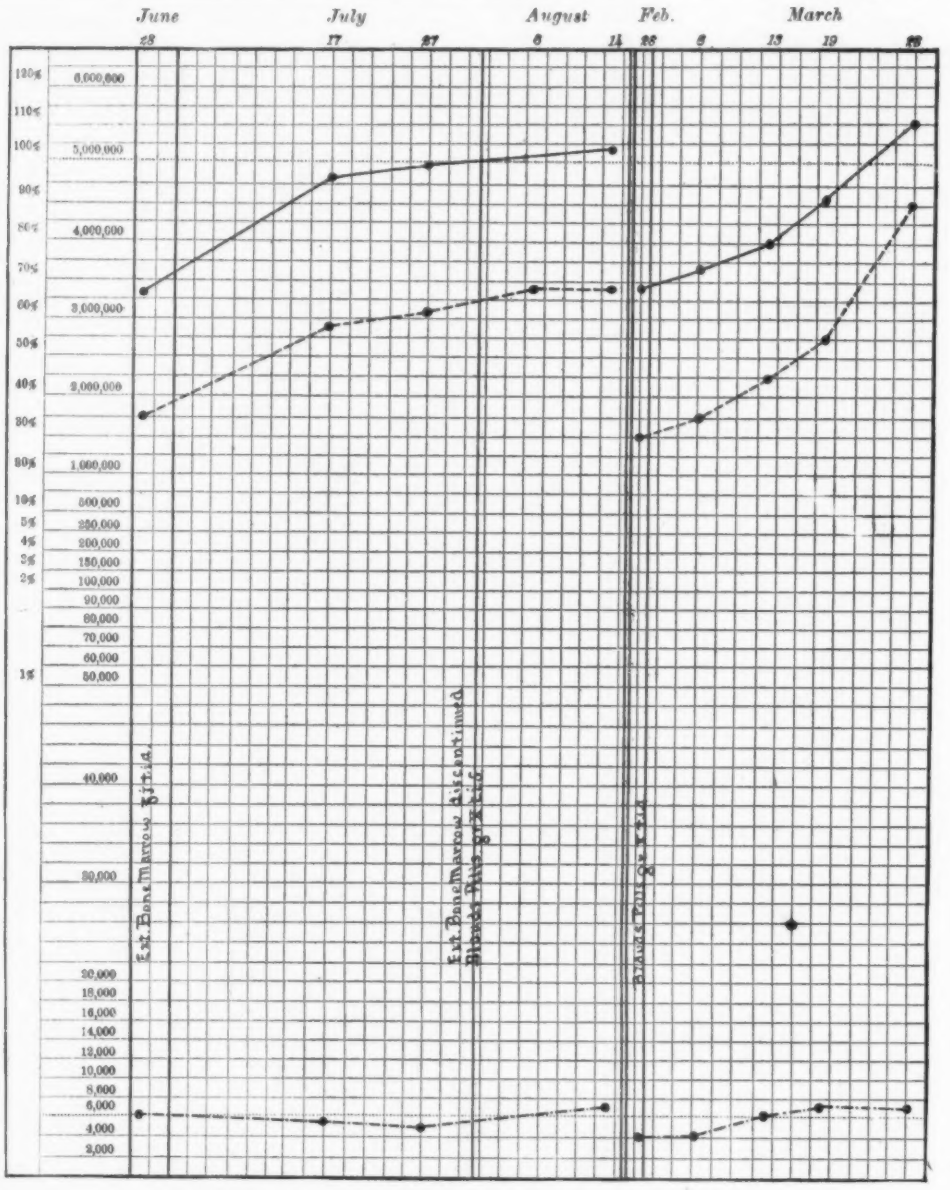


Black = red corpuscles. Broken = hæmoglobin. - - - - = colorless corpuscles.

No. 2. J. R. PERNICIOUS ANÆMIA. CASE 4.

matophilic red corpuscles. A relatively large number of nucleated red corpuscles were seen, 80 per cent. of which were typical megaloblasts, the remainder being normoblasts. A differential count of the leucocytes showed the lymphocytes to be distinctly increased (26.5 per cent.). On October 6th the blood count was, reds 1,348,000, whites, 3000; hæmoglobin 31 per cent. Up to this time the patient had had two courses of Fowler's solution, but the physiological limit of the dose had not been reached. On October 10th the extract of bone marrow was ordered, the blood count next morning being, reds 1,550,000, whites 3500; hæmoglobin 35 per cent. The marrow was continued for two weeks, during which time the patient failed visibly, the red corpuscles sinking to 822,000; hæmoglobin 18 per cent. On October 27 the extract was discontinued and Fowler's solution in increasing doses was ordered.

Stained specimens of the blood, taken on Oct. 27th, showed an interesting state of things. While the poikilocytosis, or deformity in shape and size of the red corpuscles, was markedly increased, the nucleated red corpuscles had almost entirely disappeared, only one megaloblast being seen in four specimens. Such a disappearance of the nucleated red corpuscles from the circulation may be interpreted in two ways: either the blood condition has improved to such an extent that great activity on the part of the blood-making organs is no longer necessary, or it has deteriorated so much that new formation is no longer possible. The latter condition obtained in a case of fatal purpura hæmorrhagica reported by the writer in the *Johns Hopkins Hospital Bulletin*, May, 1894. Ehrlich has also reported two cases. In the present case this was also the condition that probably prevailed. Blood count Nov. 3d, reds



Black = red corpuscles. Broken = hæmoglobin. ---- colorless corpuscles.

No. 3. J. H. Chloro-Anæmia. Case 2. E. S. Chlorosis.

900,000, whites 2000; hæmoglobin 21 per cent. Stained specimens of the blood on Nov. 3d showed about the same condition of things as on Sept. 2d. The differential count of the leucocytes is so typical that it will be given in full:

Polynuclears.	Lymphocytes.	Large mononuclears.	Trapsition.	Eosinophiles.
52.1 per cent.	32.2 per cent.	2.4 per cent.	4.2 per cent.	6.1 per cent.

Nucleated red corpuscles again appeared in the blood in relatively large numbers, 59 being seen while making a differential count of 500 leucocytes.* This reappearance of the nucleated red corpuscles may be taken as a relatively favorable sign, showing that the blood-making organs are once more active. If improvement occurs in this case under the use of arsenic it will be slow, as it requires some time to safely increase the dose to the physiological limit (20 to 25 min. t. i. d.). The general record of the case is given in chart 2.†

* This is a very convenient mode of expressing the number of nucleated red corpuscles present in a specimen of blood, but we must always take into consideration the number of leucocytes per cmm. For example, suppose case A shows 2000 leucocytes per cmm., and case B 6000. Now while making a differential count of 500 leucocytes in a stained specimen from A we see 12 nucleated reds, in a similar count in a specimen from case B we see only 4 nucleated reds. Yet the number of nucleated red corpuscles in the blood is about equal in the two cases, as in case B we cover only one-third of the ground that we do in case A.

† Since the above went to press this patient has died. A final blood count on Nov. 16, made 24 hours before death, showed only 700,000 reds, 1000 whites; hæmoglobin 17 per cent. No autopsy.

It will be seen that the two cases of chlorosis were benefited by the use of extract of bone marrow, while the two cases of pernicious anæmia were unimproved. It is difficult to understand how this remedy could be of service in cases of pernicious anæmia. Its effects can hardly be considered as analogous to those produced by thyroid extract in myxœdema. In the latter case there is atrophy of the gland, giving rise to defective secretion, so that there is an indication for attempting to supply this defect by the administration of thyroid extract. But the marrow in pernicious anæmia is, if anything, in a state of hypertrophy, and the condition is far more analogous to that of the hypertrophied and supposedly over-active thyroid gland in exophthalmic goitre than to that of the atrophied gland in myxœdema. Besides, there is no proof whatever that the marrow acts as a gland in the ordinary sense of the word. The formation of red blood corpuscles by the bone marrow cannot be properly termed a secretion, it being rather a process of cell multiplication and development, and there is no proof that this process is influenced in any way by any chemical product of the marrow itself. As regards the cases reported by previous observers, two things may be noted. First, there is room for doubt that they were true cases of pernicious anæmia. Second, the patients were given arsenic together with the bone marrow. Now it is well known that some cases of pernicious anæmia do remarkably well on arsenic, and several instances of apparent cure have been reported. Such an improvement is shown in Case 3 of our series.

It is different as regards the use of bone marrow in chlorosis. The marrow contains iron in considerable quantity, and we may reasonably suppose that the glycerin extract contains sufficient iron in organic combination to be of service in chlorosis, a disease which yields so readily to iron in almost any form. Whether its value in such cases is greater than that of the various forms of iron used in medicine is doubtful. This is well shown in chart 3, where a blood chart of a case of chlorosis treated with Blaud's pills is given together with that of Case 2 of our series. The former does not suffer by the comparison. The conclusion is that the extract of bone marrow may be of value in cases of ordinary anæmia and chlorosis, such as would be benefited by iron in other forms, but that there is no proof of its being of value in cases of primary pernicious anæmia.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of October 1, 1894.

DR. KELLY in the Chair.

Prof. J. J. Abel was elected Chairman for the coming year, and Dr. J. G. Clark was made Secretary.

Prof. W. D. Miller, of the University of Berlin, delivered an illustrated lecture in the amphitheater before an audience of Baltimore physicians and dentists, on "Some Points in Oral Pathology in Relation to Diseases of the Associated Parts and to general Diseases."

Meeting of October 15, 1894.

DR. ABEL in the Chair.

Case of Hereditary Chorea.—DR. OSLER.

Dr. Osler presented the case as illustrating a somewhat unusual feature in the family form of chorea, namely, the onset at a comparatively early age.

F. T., aged 28, a native of North Ware, N. H., was admitted Oct. 6, 1894, complaining of nervousness.

His father died at 59, after an illness of two weeks' duration. His mother died when 49 years old, of a disease similar to that with which he now suffers. She had nervous twitching for as long as he can remember. The trouble grew gradually worse, so that she could not move from her chair and she finally became bedridden. He does not think that any other members of his mother's family were affected. He has had four sisters and two brothers. One brother died at the age of 32, of influenza, after he had been afflicted for eight years with the same sort of disease as the mother. The other brother and the sisters are well and strong and have no muscular twitchings.

Personal History. As a child he had the usual disorders, but he was very well and strong until the eighteenth year. He had a comfortable home upon a farm, and though of a nervous temperament and troubled with weak eyes at times, he remained very well. He had an accident to the right elbow when he was fifteen years of age. When seventeen he had occasional rheumatic pains in the joints, but which never kept him from work. He has never had gonorrhœa or syphilis.

The present trouble began when in his eighteenth year. It was first noticed as a very slight twitching of the arms and hands. The movements afterwards involved the other parts of the body—face, shoulders and legs. He thinks the latter were involved about eight months after the arms, and a little later the muscles of the face. The twitchings have persisted uninterruptedly to the present time. He has been able to work, however, until July of last year, but the involuntary movements now interfere with his doing manual labor. In 1888 he went to California for his health, having been troubled with a cough.

About three months ago he noticed that his speech was a little involved and he did not talk as readily as before. He complains that he now tires very easily.

The patient is a healthy-looking man, with normal temperature and pulse, and without any signs of trouble in the thoracic or abdominal viscera. There are movements of almost all the muscles. Those of the face are but little involved, though the angle of the mouth is occasionally twitched and the eyebrows elevated. On talking there is no special increase in the movements and articulation is not interrupted, but he says that he tires easily when he talks for any length of time. There is no tremor of the muscles of the lips or of the tongue. The head is lifted from the pillow without any tremor. There are constant, irregular movements of the trunk muscles, causing elevation of the shoulders or slight movement of the body. The arms and hands are moved in an irregular, purposeless manner, resembling closely the movements of chorea minor, though possibly a little slower. There is not a trace of inco-ordination on voluntary movement, and he can carry a glass of water to his lips quite steadily. As he sits quietly the legs are shifted or flexed, or the toes are drawn up. The gait is a little staggering; he hesitates as he starts, walking with a wide base and swaying a little. There is no wasting of any of the muscle groups, no spasm, no rigidity, and no increase in the reflexes.

Dr. Osler referred to the fact that one peculiarity of the chronic progressive chorea described by Huntingdon was the late onset.

Huet, however, in his monograph, has noted seven instances in which the disease began before the 30th year, and in Hoffmann's patient the affection began at puberty. This patient does not know the date of onset in his mother's case, but as he says that she had it for many years before her death, it evidently started with her at an unusually early period, while his brother was affected before the 25th year.

Oliver Wendell Holmes.—Dr. Osler. [Published in the October Bulletin.]

Ureterotomy.—Dr. Kelly. [To appear in December Bulletin.]

Sarcoma in the Floor of the Mouth. Excision followed by Hypertrophy of the left Submaxillary Gland.—Dr. Bloodgood.

Dr. Bloodgood presented a case of excision of a sarcoma occupying the floor of the right side of the mouth, followed in two and one-half months by hypertrophy of the left submaxillary gland, suggesting before removal, metastasis. No return of the tumor had occurred ten months after operation.

This case is reported to the society chiefly for the unique and interesting enlargement of the left submaxillary gland, which was first noticed two months after the excision of the sarcoma, and which before its removal and microscopic examination suggested metastasis.

Surg. No. 2730, aged 46, admitted to the hospital Jan. 4, 1894.

The tumor had been noticed nine months. A few weeks before admission a cyst situated to the right and beneath the tongue had been opened at the dispensary and some milky fluid evacuated. A diagnosis of ranula was made. On admission a tumor could be felt to occupy the right half of the floor of the mouth, and a fungoid mass protruded above the teeth of the lower jaw, pushing the tongue to the left and upwards. This fungoid mass was removed. Microscopic examination showed it to be a mixed cell sarcoma, it containing large round and spindle cells.

At the second operation Dr. Halsted first performed tracheotomy, ligated the right lingual artery, and then excised the tumor in one piece with a piece of the lower jaw, part of the tongue and an area of healthy tissue. The wound healed by granulation, leaving as you now see a small sinus leading into the mouth, from which a little mucous membrane protrudes; after a sufficient time a plastic operation will be done to close this fistula.

Two and one-half months afterwards he returned with a small hard tumor, occupying the region of the left submaxillary gland, which was excised. Macroscopically it did not appear like the original tumor or a metastasis, but showed the typical appearance of a salivary gland between whose acini and ducts there had been a growth of new tissue. Microscopically the normal gland tissue was seen pressed upon by a new growth of fibrous tissue and lymphoid cells, the same picture that you will see under the second microscope, viz., a section from a tumor of the left submaxillary gland removed by Dr. Finney, in which the duct was occluded by a calculus. Both of these tumors were of about the same size and consistency; the latter has more fibrous tissue and the glandular tissue shows more advanced atrophy. The calculus in the second tumor suggests that the cause of the first was an occlusion of the duct following the operation for the removal of the sarcoma.

It is now ten months since the sarcoma was excised and there is no return. Nor is there any evidence of metastasis elsewhere, the clinical and microscopic examination agreeing.

Dr. Welch.—I think there is no doubt that Dr. Bloodgood is correct in his interpretation of the two specimens under the microscope. The one in which the calculus lodged in the duct of the submaxillary gland is, of course, a specimen of chronic inflammation of the gland. That is not an uncommon result of the occlusion of the duct of any secreting gland. There is marked atrophy of the glandular substance; the ducts and acini of the gland are fewer in number, and the connective tissue is quite rich in small round cells. It is, of course, a remarkable coincidence that in this man with sarcoma of the tongue, the submaxillary gland should have enlarged and given rise to the suspicion that it was a metastasis. When one compares the microscopical sections he will at once be struck with the identity of the two. I should think it quite possible that in the operation the duct was cut off, or that afterwards it was closed by the cicatricial tissue. The appearance is so alike in both cases that one would be inclined to think that they were due to the same cause. There is atrophy of the gland tissue and subsequently a new formation of connective tissue. The usual explanation of this condition is that there is primarily a degeneration and atrophy of the glandular part and a secondary new growth of connective tissue. It belongs to the same group as certain cases of cirrhosis of the liver that follow occlusion of the bile-ducts with gall-stones, where we have a primary atrophy and degeneration of the liver tissue and a secondary growth of new tissue.

A Case of Typhoid Septicæmia associated with Focal Abscesses in the Kidneys, due to the Typhoid Bacillus.—Dr. Flexner.

Dr. Osler.—This case was of a great deal of interest clinically, belonging to a special group of typhoid cases in which the diagnosis is usually made of meningitis, either cerebral or cerebro-spinal. The patient, a colored girl, was admitted after two weeks' illness. She was delirious, had moderately high fever, and within a day after her admission she began to have retraction of the head and rigidity of one arm, and a general hyperæsthesia. There were no retinal changes; the abdomen was somewhat swollen, and the spleen could be readily felt. It was impossible to say whether she had any rash or not. Until a day before her death we had no suspicion of typhoid. The history was very imperfect, and we regarded the case as one of meningitis—probably, as she was an emaciated colored girl, tuberculous in its nature.

Another very interesting peculiarity favored the view that it was tuberculous. After three or four days the fever fell and she had low and subnormal temperatures for four days before her death. The day before her death she developed a parotitis on the left side, and then Dr. Thayer suggested that the case was one of typhoid fever, although up to that time we had no suspicion of it. Her symptoms were entirely cerebral and cerebro-spinal—retraction of the head, muscular twitching, great rigidity of the right arm, and great increase in the reflexes. Had an autopsy not been made we certainly would not have been able to say definitely of what disease she died. Many of the cases of typhoid fever with cerebro-spinal symptoms are overlooked and put down in the death list as meningitis.

Dr. Flexner.—The results of the autopsy and the bacteriological study of the case, the clinical features of which Dr. Osler has just given you, leave no doubt as to its nature. The intestine showed several typhoid ulcerations, the first one being about 200 cm. above the valve. This one had a clean base. Larger ulcers occurred lower down, the largest being just above the valve and these presented a sloughy appearance. The large intestine also contained a number of small ulcerations. The mucous membrane of the intestine was greatly injected and actual hemorrhages had taken place into it.

The interest of the case centres in its bacteriological features. In the first place, it presents a rare condition, namely, a general infection of the body with typhoid bacilli. This organism was cultivated not only from the mesenteric glands, spleen, liver, bile, kidneys, lungs and bone marrow, but from the heart's blood itself, which contained it in considerable numbers.

In the kidneys there were a number of smaller and larger opaque white areas, the smaller hardly larger than a miliary tubercle, the larger measuring 4 mm. in width at the surface, beneath the capsule and extending downwards into the pyramids. These areas proved upon study to be definite abscesses. The contents, exam-

ined by means of cover-slip preparations, showed as the only organism present, bacilli having the form and staining properties of the typhoid bacillus. Cultures from such a nodule gave only the typhoid bacillus; and sections through the foci showed a purulent infiltration of the kidney substance corresponding to which many masses of bacilli could be distinctly seen. The bacilli occurred in clumps in the tubules, and they could be followed in several instances through the glomerular capillaries into the capsular space, whence they easily find their way into the tubules. The bacilli were easily demonstrated by means of Lœffler's methylene-blue stain, and they were readily and completely decolorized by Gram's method. In sections treated by the Gram method no other micro-organisms could be found. Had other organisms been present in these foci of suppuration they would doubtless have been demonstrable by one of the methods employed. Hence it seems that the objections urged so persistently by E. Fraenkel and Baumgarten against regarding the typhoid bacillus as a pus-producer, can in this instance be entirely excluded.

The means employed for the recognition of the typhoid bacillus in these cultures were those now regarded by most bacteriologists as sufficient to prove the identity of the organism. They were, in addition to the growths upon gelatine, agar-agar and potato, the milk, indol and fermentation tests. As you know, contrary to the B. coli communis, the typhoid bacillus does not coagulate milk, produce indol or ferment sugar.

Had the urine been examined in this case it is probable that the typhoid bacillus would have been found in it.

The parotitis mentioned by Dr. Osler was due to the streptococcus pyogenes which was present in the ducts and acini of the gland. There was a purulent infiltration of the gland.

DR. WELCH.—This is a very carefully worked out case and an important one. The question arises why in this case there should have been such a very large number of typhoid bacilli in the blood as to justify calling it a genuine septicæmia, whereas ordinarily there are no typhoid bacilli or so few demonstrable in the blood that no one would think of applying the term septicæmia to the disease. It is a well-known fact that human beings are much less subject to those bacterial infections which are common in lower animals in which the blood is crowded with myriads of these organisms. Now and then we do meet just such conditions in human beings, and this is an example. We have seen two or three cases of acute lobar pneumonia in which the blood was full of the lanceolate diplococci of pneumonia, just as it is in an inoculated rabbit. In this instance we may imagine one of two things to have existed, either that the typhoid bacillus was of very unusual virulence so that it could overcome the bactericidal power of the blood, or, what is more probable, that something had altered the bactericidal power of the blood so as to admit of the multiplication of the typhoid bacillus in the blood. The reason that the typhoid bacillus does not flourish in the blood is that the human blood is distinctly germicidal to it. If you inoculate fresh human serum with typhoid bacilli, thousands of the bacteria are quickly killed. We may therefore suppose that something has destroyed the bactericidal power of the blood. I would refer here to a communication that was made to this society last year on the action of rattlesnake poison on this very property of the blood, in which it was shown that the venom of the rattlesnake destroys the bactericidal power of the blood so that ordinary putrefactive bacteria will multiply readily in that fluid.

This case is, moreover, a conclusive one that the typhoid bacillus is capable of producing genuine abscesses. That is a matter very much disputed, especially by E. Fraenkel and Baumgarten.

As regards the very long viability of the typhoid bacillus in the human body, we have the best examples in those cases of periostitis and osteomyelitis which occur many months and even years after typhoid fever. One of the first observations as to the long duration of life of the typhoid bacillus in the animal body was made by Dr. Blachstein, in my laboratory, in his experiments on animals, where we found that the typhoid bacillus survived in the bile of inoculated animals at least four months. Those cases of post-typhoid osteomyelitis in which genuine pus is present are usually mixed infections. Most of the abscesses in which the typhoid bacillus has been found have also been mixed cases. There are some cases of abscesses due to the typhoid bacillus exclusively, however, which stand the most severe criticism.

On the Presence of Iron in the Granules of the Eosinophile Leucocytes.—DR. BARKER. (See BULLETIN for October, 1894.)

DR. ABEL.—How long was the specimen exposed to the ammonium sulphide solution, and how strong was the solution?

DR. BARKER.—This specimen was prepared in the following way: Hydrogen sulphide was passed through ordinary liquor ammonia over night. A drop of this solution was placed on a coverslip which had been heated one and a half hours; a drop of glycerine was placed on the slide, and then the cover-glass placed upon the glycerine. When placed in the thermostat at 60° C. the glycerine keeps the solution from evaporating, and it can be left for weeks without drying. The reaction in this case appeared in six hours after treatment; that is, I looked at this at the end of six hours and it was sharply stained.

DR. ABEL.—I think this is a very interesting communication in many ways. It is of great importance to localize chemical reactions in a morphological way, and Dr. Barker has made an important contribution to the physiology of the blood with respect to these granules. We can only make conjectures in regard to the nature of the organic constituent of this iron compound; most likely, however, this constituent is of a proteid nature. There are many iron albuminates which give the ammonium sulphide reaction at once. Then again there are other albumin compounds which are decomposed by ammonium sulphide with more difficulty, requiring a longer time. The liver contains such a compound. Schmiedeberg has recently published a paper on organic compounds in which he says that if sections of the liver be exposed to ammonium sulphide solutions for some time (some period of time longer than the ordinary ferric albuminates require) they blacken, and calls attention to the fact that this is a proof of a more intimate union between the iron and the proteid constituent than is the case in the ordinary ferric albuminates. The iron is in organic combination. The liver seems to have a great amount, more than any other organ, of this proteid iron compound. An iron compound identical with that contained in the liver has been made synthetically by Schmiedeberg and his pupil Marfori. It contains as high as 8 per cent. of iron. Bunge's earlier compound, isolated from the yolk of eggs and called hæmatogen, behaves like the ferratin of Schmiedeberg in being only slowly decomposed by ammonium sulphide. It is, however, a nucleo-compound, contains only 29 per cent. of iron, a little less than is contained in hæmoglobin, and is undoubtedly a more or less direct precursor of the hæmoglobin of the chick's blood. From the standpoint of physiological chemistry it would be most interesting to know more of the nature of the iron-containing compound shown by Dr. Barker to exist in the eosinophilic granules.

NOTES ON NEW BOOKS.

PHYSIOLOGICAL PAPERS OF PROF. MARTIN.

It is proposed to collect the physiological papers and addresses of Professor Martin and publish them as one of the memoirs of the Biological Laboratory of the Johns Hopkins University. This plan has been adopted in response to suggestions from a number of his former pupils, that the long and valuable services of Professor Martin to the University and his brilliant contributions to American physiology and biology should be commemorated by a memorial of

some kind. After consultation with a number of his friends it has been decided that the most appropriate form of memorial will be the publication in a handsome volume of his scientific papers and addresses. We hope to raise a fund among his friends sufficiently large to meet the cost of an edition of about 300 copies. One copy will be sent to each person or institution subscribing ten dollars, and, if desired, an extra copy for every additional ten dollars subscribed. A brief statement will be made upon the reverse of the title-page or elsewhere, to the effect that the volume is published by his friends and former pupils, and probably a list of subscribers will be appended. As the work will be placed at once in the hands of the printer, it is requested that subscriptions be sent promptly, in the form of checks or money orders made payable to Professor W. H. Howell, Johns Hopkins University, Baltimore.

The following provisional list contains the titles of papers which will appear in the collection; they are here arranged in chronological order:

Notes on the structure of the olfactory mucous membrane. [*Studies from the Physiological Laboratory in the University of Cambridge, Part I*, 1873.]

The study and teaching of Biology. [*Popular Science Monthly, Jan.*, 1877.]

The normal respiratory movements of the frog, and the influence upon its respiratory centre of stimulation of the optic lobes. [*Journal of Physiology*, 1878.]

The influence of stimulation of the mid-brain upon the respiratory rhythm of the mammal—with W. D. Booker. [*Journal of Physiology*, 1878.]

On the respiratory function of the internal intercostal muscles——with E. M. Hartwell. [*Journal of Physiology*, 1879.]

The physiology of secretion. [*Annual address delivered before the Medical and Chirurgical Faculty of Maryland, April* 9, 1879.]

A self-feeding chronographic pen. [*Studies from the Biological Laboratory, J. H. U.*, 1880.]

Observations upon the mean pressure and the character of the pulse wave in the coronary arteries of the heart—with W. T. Sedgwick. [*Journal of Physiology*, 1881.]

A new method of studying the mammalian heart. [*Studies from the Biological Laboratory, J. H. U.*, 1881.]

Observations on the direct influence of variations of arterial pressure upon the rate of beat of the mammalian heart. [*Studies from the Biological Laboratory, J. H. U.*, 1882.]

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Vaso-motor nerves of the heart—with D. J. Lingle. [*Transactions of the Medical and Chirurgical Faculty of Maryland*, 1891.]

Some experiments as to the physiological effects of "differential respiration"—with G. P. Dreyer. [*Studies from the Biological Laboratory, J. H. U.*, 1893.]

A Practical Manual of Mental Medicine. By Dr. E. Régis, Professor of Mental Diseases, Bordeaux. With a preface by M. Benjamin Ball. Second edition, thoroughly revised and largely rewritten. Authorized translation by H. M. Bannister, A. M., M. D. (*Utica, N. Y.: Press of American Journal of Insanity*, 1894.)

As the author pleasantly remarks in his introduction to the American translation, "It is the first instance of a work treating of mental alienation, written by an alienist, translated by an alienist, and, under the direction of an alienist, printed and bound by the insane." The book is a good one, well translated and neatly and tastefully printed. It is modestly called by the author a "Manual," but it is much more than that, and is indeed a full and satisfactory text-book. As a rule, the definitions are clear and self-explanatory, but occasionally they seem open to the charge of over-refinement. Take for example the attempt to show a difference between mental alienation and insanity. Mental alienation, according to the author, is "the total of pathological conditions essentially characterized by disorders of the intelligence," while insanity "is a special disease, is a form of alienation characterized by the accidental, unconscious and more or less permanent disturbance of the reason." According to this reasoning, mania and many conditions of paranoia are not insanity. In our opinion it is impossible to distinguish in this manner between disorders of the *intelligence* and disorders of the *reason*. Disorders of the intelligence, of the emotions and of the will are to be considered insanity equally with disorders of the reasoning powers.

It is gratifying to perceive that he places among the causes of insanity solitary confinement. The effect of this form of prison life is unmistakably to produce insanity, and it should be more frequently recognized by alienists. His characterization of a remission as an attenuation of the disease is a happy one and commends itself to all who have seen cases of circular insanity. The chapter on pathological anatomy is unsatisfactory and does not adequately represent our present state of knowledge.

The chapters on the "Degeneracies of Evolution," "Degeneracies of Involution," and "Insanities associated with Physiological Conditions," are especially valuable. The subject-matter has not been as clearly presented in English before.

The book should be in the hands of every physician who sees cases of insanity.

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